

# Notice of Allowability

Application No.

09/778,388

Examiner

Richard Schnizer, Ph. D

Applicant(s)

SZOKA ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 10/18/04.
2. ☒ The allowed claim(s) is/are 1,2,5-7 and 10-52.
3. ☒ The drawings filed on 07 February 2001 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All b) ☐ Some\* c) ☐ None of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
  6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
    - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
    - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

## Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date \_\_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Nathan Koenig on 11/3/04.

The application has been amended as follows:

In claims 30 and 48, delete "min", and substitute --minutes-- therefor.

Claim 50 (currently amended). A method for gene transfer comprising the steps of:

- a) providing an encapsulator comprising a low pH sensitive lipidic composition having an amphipathic characteristic, an acid labile orthoester bond and a polynucleotide, wherein the encapsulator exhibits degradation of less than 10% within 3 hours at a pH of 7.4 and degradation greater than 50% within 60 minutes at a pH of 5.0, and wherein hydrolysis and cleavage of the orthoester [[linker]] bond directly detaches a hydrophilic portion of the lipidic composition from a hydrophobic portion of the lipidic composition and the encapsulator to eliminate the amphipathic characteristic and destabilize the encapsulator;
  - b) administering the encapsulator to an animal;
  - c) exposing the encapsulator to a reduced pH to degrade the encapsulator;
- and

d) releasing the polynucleotide.

The following is an examiner's statement of reasons for allowance: Prior to this Action, claims were rejected as anticipated by Nantz (US Patent 6,200,599), or obvious over Nantz in view of various secondary references. Nantz was relied upon to teach lipid formulations (liposomes, micelles, lipidic aggregates) comprising orthoester lipids with a hydrophobic lipidic portion joined to a hydrophilic head group comprising an ammonium ion, and methods of delivering the composition to cells in vivo under conditions that result in acid catalyzed hydrolysis of the orthoester, and destabilization of the aggregate. See e.g. column 2, line 44 to column 3, line 18, column 5, lines 53-56, and column 12, lines 13-17. Note that in Formula I at column 2, A and A1 may be oxygen, R2 may be an alkoxy group, and (CH<sub>2</sub>)<sub>x</sub> and (CH<sub>2</sub>)<sub>y</sub> attach to the orthoester a hydrophilic head group (ZQR4). As a result, the structure of Nantz is analogous to the structure set forth by applicant in instant Fig. 2.

However, Applicant has pointed out that the structures of Nantz differ from the instantly claimed structures in that the structures of Nantz must have two hydrophobic tails, i.e. R1 and R2. As a result, the loss of amphipathic character required by the instant claims does not occur as a direct result of orthoester hydrolysis, instead orthoester hydrolysis of the structure of Nantz directly eliminates one hydrophobic tail yielding a compound that is still amphipathic because it retains both a hydrophilic portion and a hydrophobic tail. In contrast, the instant application does not disclose or claim such structures, disclosing instead amphipathic structures with a single

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hydrophobic tail, wherein orthoester hydrolysis must result directly in separation of the hydrophobic and hydrophilic groups, resulting in a direct loss of amphipathic character.

### ***Conclusion***

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.

DAVE T. NGUYEN  
PRIMARY EXAMINER

